

# <sup>99m</sup>Tc-Ethylenedicysteine-folate

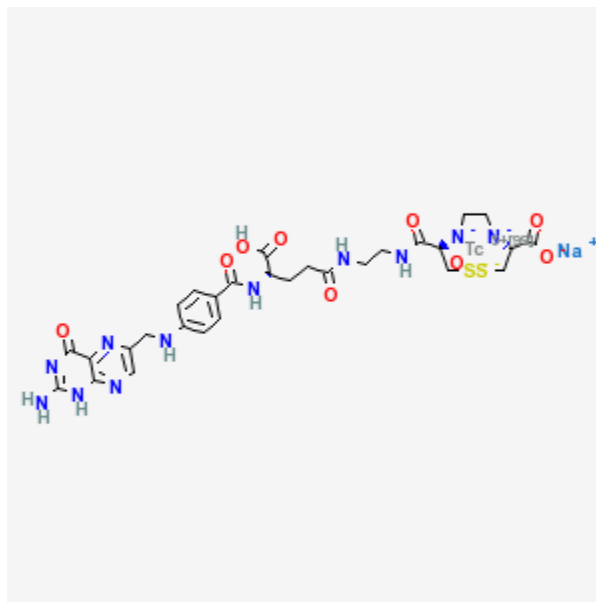
## <sup>99m</sup>Tc-EC-folate

Created: April 18, 2005

Updated: May 19, 2005

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<b>Chemical name:</b>	<sup>99m</sup> Tc-Ethylenedicysteine-folate
<b>Abbreviated name:</b>	<sup>99m</sup> Tc-EC-folate
<b>Synonym:</b>	
<b>Backbone:</b>	Folic acid
<b>Target:</b>	Folate receptor
<b>Mechanism:</b>	Receptor binding
<b>Method of detection:</b>	SPECT
<b>Source of signal:</b>	<sup>99m</sup> Tc
<b>Activation:</b>	No
<b>In vitro studies:</b>	Yes
<b>Rodent studies:</b>	Yes
<b>Other non-primate mammal studies:</b>	No
<b>Non-human primate studies:</b>	No
<b>Human studies:</b>	No



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## Background

[PubMed]

Folic acid is a water-soluble B vitamin (1). It is essential for methylation and DNA synthesis. The primary pathway for entry of folate into cells is through a facilitated transporter, which has a low affinity for folate with  $K_m$  of 1-5  $\mu\text{M}$ . Some cells in the choroid plexus, kidney, lung, thyroid, spleen, placenta, and thymus also possess a higher affinity ( $K_d$ , 0.5 nM) receptor that allows folate uptake via receptor-mediated endocytosis. Some human epithelial tumor cells were found to overexpress folate-binding protein (2). More than 90% of human ovarian and endometrial cancers express the high-affinity receptor, which is absent in normal tissues. Breast, colorectal, renal, and lung carcinomas also overexpressed the folate receptor but to a lesser frequency (20-50%). <sup>99m</sup>Tc-EC-folate was synthesized and developed as a folate receptor imaging agent (3).

## Synthesis

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[PubMed]

L,L-Ethylenedicysteine (EC) was conjugated to folate-NH<sub>2</sub> using sulfo-*N*-hydroxysulfosuccinimide (3). One EC residue (268 Da) was estimated to conjugate to folate-NH<sub>2</sub> (483 Da) to form EC-folate. <sup>99m</sup>Tc was complexed efficiently to EC-Folate to form <sup>99m</sup>Tc-EC-folate with a radiochemical purity of >95%. The specific activity was calculated to be about 0.37 MBq/μg (10 μCi/μg) before *in vivo* injection to rats.

## In Vitro Studies: Testing in Cells and Tissues

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<sup>99m</sup>Tc-EC-folate was found to be stable in dog serum samples at 37°C for up to 4 h (3).

## Animal Studies

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### Rodents

[PubMed]

Rats were inoculated with rat mammary tumor cells, followed by intravenous injection (0.37 MBq/rat, 10 μCi/rat, 10 μg/rat) of <sup>99m</sup>Tc-EC-folate or <sup>99m</sup>Tc-EC 14 -17 days after tumor transplantation (3). Tumor-to-blood uptake ratios for <sup>99m</sup>Tc-EC-folate rats increased as a function of time, whereas these ratios decreased for <sup>99m</sup>Tc-EC in the same period. Tumor uptake in <sup>99m</sup>Tc-EC-folate rats was about 1-fold higher than <sup>99m</sup>Tc-EC rats. The kidneys and liver were the organs with high uptakes of both tracers. Both tracers were excreted mainly in the urine. Co-injections of rats with 0.15 mol/kg of unlabeled folate blocked the uptake of <sup>99m</sup>Tc-EC-folate by 30%.

Scintigraphic images of rats given <sup>99m</sup>Tc-EC-folate (18.5 MBq/rat, 0.5 mCi/rat, 50 μg/rat) showed that tumors in the right hind legs could be well visualized at 1-4 h (3). <sup>99m</sup>Tc-EC-folate could be a useful tool for imaging folate receptor-positive tumors.

### Other Non-Primate Mammals

[PubMed]

No publication is currently available.

### Non-Human Primates

[PubMed]

No publication is currently available.

## Human Studies

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[PubMed]

No publication is currently available.

## References

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1. Stanger O. Physiology of folic acid in health and disease. *Curr Drug Metab* 3:211–223; 2002. (PubMed)
2. Ke CY, Mathias CJ, Green MA. The folate receptor as a molecular target for tumor-selective radionuclide delivery. *Nucl Med Biol* 30:811–817; 2003. (PubMed)
3. Ilgan S, Yang DJ, Higuchi T, Zareneyrizi F, Bayhan H, Yu D, Kim EE, Podoloff DA. <sup>99m</sup>Tc-ethylenedicysteine-folate: a new tumor imaging agent. Synthesis, labeling and evaluation in animals. *Cancer Biother Radiopharm* 13:427–435; 1998. (PubMed)